ERYTHROCYTES


Hemoglobin Bart's, in concentrations ranging from 1 to 6%, was found in cord blood of 17% of Yemenite and 11% of Iraqi newborn infants. This finding identifies the two populations as having a high carrier rate of α-thalassemia. As a group, infants with Hb Bart's at birth tended to have a relatively high red cell count, a lower Hb concentration, and lower MCV, MCH, and MCHC values. Two groups, one in which the concentration of Hb Bart's ranged between 1 and 3% and a smaller group with a 5-6% concentration of the abnormal hemoglobin, could be distinguished. No recognizable α-thalassemia was found in a random sample of 100 Yemenite children, aged 2-12 yr. In 19 out of 35 families of infants with Hb Bart's at birth, at least one additional family member showed hematologic findings compatible with α-thalassemia. Hb H disease is the most severe expression of α-thalassemia found in Yemenite and Iraqi Jews, while Hb Bart's hydrops fetalis, known to occur in Southeast Asian populations with α-thalassemia, has not yet been observed. It is suggested that in Yemenite and Iraqi Jews, Hb H disease represents the homozygous state for a more severe defect, associated with a concentration of Hb Bart's of 5-6% at birth. The heterogeneity of α-thalassemia syndromes in different populations is illustrated by our findings. On the other hand, the dual pattern in concentrations of Hb Bart's in Yemenite and Iraqi Jews is similar to that observed in Thailand. The pattern of coexistence within each population of a stronger and a milder defect has now been shown to apply to at least three genetically unrelated populations: Thais and Yemenite and Iraqi Jews. It probably represents a universal phenomenon having a common mechanism.—B.R.

Chromosome Studies in Fanconi’s Anemia Before and After Treatment With

Two unrelated patients with Fanconi’s anemia showed chromosome changes like those previously described in culture of PHA-stimulated lymphocytes. After administration of large doses of oxymetholone for nearly 6 mo to one patient, the chromosome abnormalities disappeared almost entirely, but there was little change in the clinical or hematologic status. By contrast, the second patient had had long-term treatment with small doses of anabolic steroids and was hematologically normal, but the chromosomes showed gross changes—F.W.G.

LEUKOCYTES


Media “conditioned” by various normal and neoplastic cells were dialyzed, and the dialysates were tested for their ability to inhibit the growth of marrow colonies in vitro. Both normal and leukemic cells were found to produce dialyzable inhibitors that were heat and ether resistant and were not species specific. Since the inhibitor derived from normal cells was active against leukemic cells and the inhibitor derived from leukemic cells was active against normal cells, the results argue against the suggestion that the important abnormality in leukemia is failure to produce an inhibitor or resistance to an inhibitor.—A.A.M.


Three males with a variable proportion of 45,X cells in their bone marrow were observed among 100 males examined. All three were found in a group of 37 males who had some hematologic disorder. No Y-minus males were observed in a group of 37 males who had other, nonhematologic disorders, or among six volunteers. Quinacrine fluorescence was used to identify precisely the missing small acrocentric chromosome as the Y. One of the three males with a Y-minus cell line was 55 yr of age; the other was 60 yr. All three males had thrombocytopenia that had been treated with prednisone, and two had undergone splenectomy. One of the cases has shown a disappearance of his aueploid cells over a 14-mo period. One other case has shown an increase in the proportion of 45,X cells during a 2-yr interval. The new technique of quinacrine fluorescence, together with Giemsa staining (banding), permits precise identification of chromosomes. An important new era in chromosome analysis as applied to hematologic disorders is now opening.—J.E.U.


Activity of acid phosphatase in granulocytes of peripheral blood and of aseptic dermal exudates was investigated in patients suffering from rheumatoid arthritis, as well as in patients with degenerative changes of the joints. It was found that large doses of vitamin A decreased the intensity of cytoenzymatic reactions for acid phosphatase in granulocytes, whereas pretreatment with Arequine inhibited this effect.—M.K.

The authors investigated the activity of alkaline phosphatase in granulocytes (G.A.P.) in 425 cases of internal diseases not involving the hematopoietic system. The increase of G.A.P. in the acute stage of rheumatoid arthritis was confirmed. In cases of myocardial infarction, the rise in G.A.P. depended on the presence of shock, the extent of the infarct, and inflammatory complications. In liver diseases, the increase of G.A.P. was noted mostly in primary and metastatic carcinoma. In cases of neoplastic diseases, the increase of G.A.P. depended on the extent of the pathologic changes and not on the localization of the primary lesion. In early stages of disease, no changes in G.A.P. activity were found.—M.K.

Investigation of the DNA and RNA Content of Lymphocytes in Cases of Chronic Lymphocytic Leukemia. R. Fidelski, Z. Walter, J. Judykiewicz, and E. Krykowski. Faculty of General and Experimental Pathology, Military School of Medicine, Faculty of Biochemistry, University of Lodz and 2nd Department of Internal Medicine, School of Medicine, Lodz, Poland. Acta Haemat. Pol. 2:149–153, 1971.

The content of nucleic acids in leukocytes, as well as in isolated lymphocyte fractions, from patients with chronic lymphocytic leukemia (CLL) was determined and compared with the values found in normal subjects and in patients with rheumatoid arthritis. The results were analyzed with regard to the course of the CLL. It was found that in patients with a mild course, the RNA content was near the normal value, in patients with a malignant course and an increased WBC it was increased, while in patients under cytostatic treatment and decreased WBC, the RNA content was lowered.—M.K.


The application of gelatin sedimentation method for isolation of mononuclear and polymorphonuclear leukocytes from normal human peripheral blood is described. Using this method, preparations of mononuclear cells of 98% purity and of polymorphonuclear cells of 85–90% purity were obtained, while the total recovery leukocytes ranged from 95 to 98%. M.K.


In two patients with chronic lymphatic leukaemia in whom the serum contained neither monoclonal IgM nor free \( \mu \) chains, immunofluorescence studies demonstrated the presence of accumulated intracytoplasmic material reacting with antisera to \( \mu \) chains and only to one type of light chain. These patients are cited as examples of secretory immunoproliferative disorder characterized by unreleased monoclonal immunoglobulin marker.—J.M.B.


A series of 1467 white patients with nondisseminated lymphomas of extranodal origin was taken from data collected by the End Results Group of cancer registries in the years 1950–1964. Excluding Hodgkin’s disease, about one-fourth of the lymphomas reported arose in sites other than lymph nodes. Survival rates and distributions are listed for site of origin, major histologic types, sex, age, and extent of disease. For the more frequently reported sites, survival rates are given according to the type of initial treatment used. The prognosis of patients with extranodal lymphomas is compared with that for “all cancers” of the same site, and the lymphoma patients appear to fare appreciably better when the site of origin is stomach, lung, or tonsil.—J.E.U.

The authors determined the proteolytic activity of leukocytes in 26 patients treated with radium because of neoplasms of the uterine cervix. The proteolytic activity was determined using casein labeled with radioactive iodine $^{131}I$. A significant increase of the proteolytic activity was found in the leukocytes after termination of this treatment, with return to normal values 7 days after the end of treatment.—M.K.


Activities of acid phosphatase, acid protease, and neutral protease were investigated in subcellular fractions of granulocytes from patients with RA, LE, and AS, as well as from a control group of healthy people. Decreased activities of all the examined enzymes was demonstrated in the lysosomal fraction in RA, LE, and AS.—M.K.


Using casein labeled with $^{131}I$, the authors determined proteolytic activity of lymphocytes isolated from normal human blood. It was found that lymphocytes exhibit proteolytic activity, that is significantly higher in homogenates than in the intact cells. Optimum pH was found to lay between 8.2–8.6. Proteolysis of casein by lymphocyte homogenates was enhanced by streptokinase and inhibited by $5 \times 10^{-4} M$ epsilon-aminocaproic acid but not by soy bean trypsin inhibitor (0.2–150 $\mu g/ml$). When lymphocyte and granulocyte homogenates were compared, the activity of the latter was found to be markedly higher.—M.K.


Patients with Sjogren’s syndrome are described in support of the view that in these subjects there is a wide spectrum of lymphoproliferative activity, ranging from those with lymphoid infiltrates confined to glandular tissue to those with widespread lymphoreticular malignancy. In the middle is a group in which the proliferative process apparently has the potential to regress under therapy or to progress to frank neoplasia.—J.M.B.


The major part of endogenous vitamin B$_{12}$ in the serum is bound to an a-globulin fraction, transcobalamin-I. Small amounts of B$_{12}$ are bound to a b-globulin fraction, transcobalamin-II. In chronic myeloid leukemia, there is an increase in transcobalamin-I production, and large amounts of B$_{12}$ are bound to this protein. The B$_{12}$ bound to transcobalamin-II remains within the normal range. There is no correlation between the peripheral white cell count and transcobalamin-I binding capacity. Following chemotherapy with busulfan (Myleran), there is a gradual decrease in the binding capacity of transcobalamin-I. Cytotoxic drugs, such as 6-mercaptopurine, asparaginase, and cytosine-arabinoside, produce a more rapid decrease in transcobalamin-I binding capacity. The effect of cytotoxic
ABSTRACTS

Drugs on the binding of vitamin B12 by transcobalamin-I in myeloid leukemia may serve as a useful criterion in the evaluation of the therapeutic effect of these drugs.—B.R.


Information relating to 978 children who died before their 15th birthday from leukemia in Scotland (1939–68) was analyzed. Mortality from leukemia increased during the 1940’s and 1950’s but declined slightly during the 1960’s. The mortality from lymphatic disease was highest at 3 and 4 yr of age but from the myeloid and monocytic varieties was evenly distributed throughout the first 14 yr. The leukemia mortality in Scotland was lower than in most other countries and there was no evidence of urban-rural gradient or of seasonal variation of onset or mortality, or of clustering of cases. Regional variations in mortality from childhood leukemia were not significant.—J.M.B.


The MOPP regime of combination chemotherapy was used to treat 55 patients with advanced Hodgkin’s disease, 44 of whom had stage 4 disease and 11 of whom had stage 3 disease. Forty-nine of the patients had previously been treated with irradiation and/or chemotherapy. Six courses of treatment were given at monthly intervals, a seventh after a further 2 mo, and subsequent courses were given at 3-mo intervals. Forty-six patients had a complete remission and three a partial remission. The median length of remission was estimated at 28 mo from the onset of treatment. Poorer response was shown by patients whose tissue biopsy showed more than 50% atypical histiocytes and by those whose previous treatment included both radiotherapy and chemotherapy.—A.A.M.


Diagnostic laparotomy has been used as a staging aid after complete medical evaluation of 15 patients with non-Hodgkin’s lymphoma. The stage of disease was altered by the surgical procedure in seven of the 15 patients and is recommended for all patients with stages I, II, or III non-Hodgkin’s lymphoma. In patients with lymphoma, this procedure appears to be even more rewarding than in patients with Hodgkin’s disease.—J.E.U.


The authors performed laparotomy and splenectomy for 40 patients with untreated Hodgkin’s disease as part of the initial diagnostic evaluation. Approximately 25% of patients who were felt to have disease limited to above the diaphragm, on the basis of the initial clinical and laboratory examination (including lymphangiography), were found to have abdominal disease on surgical exploration. Of the patients with abdominal disease, 75% had histologically involved spleens that were seldom detected preoperatively. In none of these patients was the liver involved. About 50% of our patients with abdominal disease failed to have a contiguous pattern to their sites of involvement, which suggests that Hodgkin’s disease may be multicentric in origin in some patients. The therapeutic benefits of splenectomy are also detailed. This operation appears to be a valuable procedure in the evaluation of patients with Hodgkin’s disease and their subsequent management and expectation of cure with radical radiotherapy. This study, together with others previously published, document the value of diagnostic laparotomy and splenectomy in staging Hodgkin’s disease.—J.E.U.

Treatment of Lymphoreticulosarcoma. Z. Singer, J. Japa, K. Rozek, and I. Januszewska. First Department of Internal
ABSTRACTS

Ninety-two cases of lymphoreticulosarcoma were observed and 72 of them were treated. Most patients were in severe conditions with generalized disease (74 cases). The best therapeutic results were obtained with radiotherapy, in 12% of cases. Treatment with cytostatic agents (most frequently with cyclophosphamide) was given to 17 patients, including 26 cases in which radiotherapy was given concurrently. Very good immediate therapeutic results were seen in 46% of cases, good in 29%, while no effect was obtained in 10% of cases. Fifteen per cent of patients died during treatment. The mean survival was shorter in patients treated with cyclophosphamide than in those treated with radiotherapy, or with radiotherapy and cyclophosphamide.—M.K.

HEMOSTASIS


This study has been undertaken to demonstrate the correlation between the proliferation of cancer cells and the increase of fibrinogen and its derivatives in the body fluids. The concentration of plasma fibrinogen in patients with cancer increased in parallel with the growth of cancer and markedly decreased after surgical extirpation of tumor tissues. Fibrinogen level in pleural and ascitic fluids was estimated by use of the single, radial immunodiffusion method. The mean value of fibrinogen for 27 cancer cell positive fluids was 160 mg/dl, compared to 51 mg/dl of 29 negative samples. The immunoelectrophoresis, used for characterization of fibrinogen and detection of fibrinogen degradation products, was performed with antihuman fibrinogen antiserum. The reaction patterns have been classified into five types, and their relation to morphologic characteristics of cellular components in the fluids has been investigated. The cancerous fluids were involved in types IV and V. Most of inflammatory effusions belonged to type III and the transudates caused by liver cirrhosis or other diseases to types I or II, forming very weak patterns. It may be assumed that the chemical and immunologic analysis of fibrinogen and its derivatives in the body fluids is useful for the diagnosis or differentiation of cancerous and other disorders—K.F.


The inhibiting activity on blood coagulation by a new synthetic antiplasminic substance having a chemical structure of 4-(2-carboxyethyl) phenyl-trans-4-aminomethyl cyclohexane carboxylate hydrochloride was studied in vitro. The substance exerted a highly potent inhibiting activity on thrombin. The kinetic study employing the technique of Lineweaver and Burk revealed that the inhibition was competitive in type. In addition, it is suggested that the substance might inhibit the process of the first phase of blood coagulation concerning the activation of factors IX and X.—K.F.


Description of a new method for obtaining a highly active factor VIII concentrate is given. Eight portions of cryoprecipitate mixed with dextran yielded a preparation containing 650 AHG units in a volume of 50–60 ml. The degree of factor VIII purification, as measured against the protein, was 54. The preparation, designated as fraction C-1, did not lose its activity when stored in the frozen state. No side effects were observed after infusion of the preparation, and the clinical results were good.—M.K.
ABSTRACTS


Citrated platelet-free noncontact plasma, if subjected to prolonged dialysis, is altered in regard to its behavior in the presence of a glass surface. Unlike native or citrated plasma, dialyzed plasma was insensitive and could be incubated in glass apparatus with little or no contact activation; the amount of change was related to the duration of dialysis. If ionized calcium in low concentration was added to the dialyzed plasma, contacting occurred, and coagulation subsequent to full recalcification was accelerated. —M.B.


Of three techniques for the measurement of fibrin degradation products (FDP), the tanned, red cell hemagglutination inhibition immunooassay was the quickest and most useful, the radial immunodiffusion method the most accurate at high FDP levels, and the precipitin test valueless. Half of 80 patients with thromboembolic disorders had abnormally high levels of FDP, and thus FDP measurements may be of some value in the diagnosis of such disorders. —F.W.G.


The proteolytic activity connected with alpha2-macroglobulin was studied in the serum of 350 patients in a department of internal diseases. Normal activity was found in patients without evidence of hemorrhagic diathesis treated for diseases of the digestive tract, respiratory system, cardiovascular system, and urinary tract.

A significant decrease of proteolytic activity was demonstrated in certain diseases associated with blood-clotting disturbances. They included: secondary thrombocytopenias, hemophilia and diseases with decreased synthesis of the prothrombin complex in the liver. Clinical observations suggest that determination of the proteolytic activity in the serum connected with alpha2-macroglobulin may be useful in the over-all assessment of the efficiency of the blood-clotting system. —M.K.


A simple paracoagulation reaction (PR) was used for detection of circulating fibrin. A positive reaction consisted in the formation of a precipitate or a clot from plasma after addition of protamine sulfate to a final concentration of 0.1%, at 37°C. PR was carried out 553 times for 392 patients and 36 healthy subjects. A more frequent occurrence of a positive PR was observed in the diseases in which an intravascular clotting activation may be expected. A high correlation was found between the fibrin level, platelet count, thrombelastographic indices, and PR. An evident correlation occurred between the positive PR (and its intensity) and the presence of an active coagulation process or a bleeding tendency due to intravascular clotting. The authors conclude that the paracoagulation reaction may be used as a valuable test for detection and observation of the course of intravascular activation of clotting. —M.K.

The paracoagulation reaction (PR) was studied in 100 patients undergoing operations under conditions of extracorporeal circulation. PR was measured several times in each case, i.e., before the operation, every 15–30 min during perfusion (extracorporeal circulation), and when possible, in the afternoon or in the evening after the operation, as well as on subsequent days. It was found that during the perfusion, positive PR appeared in 29% of cases showing a statistically significant correlation with the duration of perfusion and the operative blood loss. After completion of perfusion and deheparinization, positive PR was present in 77% of cases, with strikingly positive or strong reaction in 28% of cases showing a statistically significant correlation with the extent of surgical blood loss and fibrinogen level on the first day after operation. The reaction of paracoagulation may be useful for detection of activation of intravascular clotting, occurring sometimes during perfusion, and for recognition of the etiology of postoperative bleeding.—M.K.


The fibrinolytic activity was determined in euglobulins, plasma, and whole blood from patients with chronic bronchial asthma—during attacks of bronchial asthma, in the asymptomatic period, and after production of venous stasis. It was shown that a significant increase of fibrinolytic activity develops in these patients. This increase is particularly marked during an attack of bronchial asthma.—M.K.


Experimental pancreatitis was induced in dogs by injections of either bile mixed with trypsin or of a mixture of bile acids into the pancreatic duct. In the early stages of the experimental acute pancreatitis, a striking inhibition of fibrinolysis and consumption of plasminogen, antiplasmin, as well as of factor V, X and platelets was observed. Similar changes were demonstrated in the blood of 17 patients with acute pancreatitis. Lyophilized pancreatic juice was found to inhibit fibrinolytic activity of euglobulins in vitro. Treatment with heparin (200–300 mg/day) applied to seven patients for 5–7 days resulted in an amelioration of the general state, decrease of the amylase activity in blood serum, and normalization of clotting and fibrinolysis.—M.K.


A sample of 53 Indians, living in the Parque Nacional do Xingu and belonging to several tribes, were investigated for the ABO, Rh, and MN blood group systems. The antisera used in blood typing were: anti-AB, anti-A, and anti-B for ABO; anti-M and anti-N for MN; and anti-D, anti-C, and anti-E for Rh. Results revealed that individuals of the ABO system belonged (100%) to group O; of the MN system 69.8% were MM, 22.6% were MN, and 7.5% were NN. Of the Rh system 49.1% were R1R2 (CDe/cDE), 37.8% were R2R2 (CDe/cDE), 3.7% were RrR0 (cDe/cDe), and 9.4% were RrR0 (cDe/cDe). No Rh negative subjects, as well as no cde (r1), cdE (r2) or Cde (r?) were found. The data indicated that the tribes in that region are racially homogeneous.—M.J.

Transferrin types have been determined in a sample of the Polish population numbering 1300 individuals. In five persons, the phenotype varieties CDi, BiC, B2C, and Bi-2C were observed. Determination of transferrin types in the families of four of the individuals with phenotypic varieties revealed dependence of Tf types on a single genetic locus and codominance of the TfB and TfD genes in relation to the Tfc gene. Altered mobility of transferrins caused by bacterial infection may lead to false determination of transferrin types.—M.K.


Two groups of rats of the August strain were used. One received i.d. injections of Freund's adjuvant, the other served as control. Both were injected i.p. with 35S-cysteine. The label was introduced on the first, third, and fifth day in a 0.2 μCi/g of body weight dose and on the sixth day in a 0.4 μCi/g of body weight dose. On the seventh day the animals were sacrificed, and radioautographic preparations were made from smears of free cell suspensions from the peritoneal cavity, thymus, bone marrow, lymphatic nodes, spleen, and liver. In the control group, the peritoneal cavity, thymus, and bone marrow cells were labeled, and in the experimental animals the percentage of labeled bone marrow, thymus, and leukocytes of the peritoneal cavity was significantly higher than in the controls. Labeling of the cells of the draining lymph nodes was also noted in the experimental group. The results seem to indicate a particular requirement for cysteine in the cells of organs exhibiting a high proliferation rate and an increased requirement for this substance in lymphoid cells in the course of development of hypersensitivity of the delayed type.—M.K.


Of 98 patients receiving alpha-methyldopa as therapy for hypertension, 26 had a positive direct Coombs' test, 11 a positive test for antinuclear factor, and five a positive LE cell test. In a few cases, the Coombs' test was only transiently positive. One patient developed evidence of hemolysis that improved after cessation of alpha-methyldopa therapy.—A.A.M.


It is shown that the measurement of erythropoiesis as shown by 59Fe incorporation is a useful assay for graft-vs-host reaction. Irradiated hybrid mice were injected with various parental cell strains, all of which produced some depression of 59Fe incorporation, the most effective being lymph node and spleen cells. This went along with hepatosplenomegaly. Extramedullary hemopoiesis occurred, especially in the spleen, when significant numbers of hematopoietic cells were present in the inocula and the assay system was not suitable in these circumstances.—F.W.G.


Sera were taken in the course of a survey of ostensibly healthy people from 2192 adults in a New Zealand town with a total adult population of 2670. After 3 yr of storage in a deepfreeze, 11 of the sera were found to show monoclonal gamma peaks (0.5% of all individuals tested, and 1.5% of those over 70). During the 3-yr interval, two of the subjects had died from unrelated diseases, four had developed associated clinical disease (myelomatosis, Waldenström's macroglobulinemia, and
lymphosarcoma), two had blood changes suggesting early lymphoma, two had shown no obvious disease, and one had lost the monoclonal peak but had probably developed immunoparesis. Monoclonal gammanopathy appears to be a neoplastic condition with a variable rate of progression, but treatment is not indicated in the absence of symptoms.—F.W.G.


A 36-yr-old woman presented with large painful ecchymoses, suggesting the clinical picture of autoerythrocyte sensitization (AES). Intracutaneous administration of her own leukocytes was followed by hemorrhagic skin reactions. These reactions did not occur in normal subjects after injection of their own or of the patient’s leukocytes. Intracutaneous administration of synthetic bradykinin to the patient induced the appearance of ecchymoses similar to the spontaneously occurring ones. No hemorrhages appeared in control subjects under similar conditions. Low bradykininase activity was found in the patient’s leukocytes. Bradykinin-like activity was found in the perfusate taken from a painful skin area before the appearance of ecchymoses. It is assumed that the hemorrhagic skin lesions might be due to the local formation of bradykinin and a delay in its inactivation because of low bradykininase activity of the patient’s leukocytes. A similar pathogenetic mechanism has been suggested in other cases of AES and DNA sensitization.—B.R.

MISCELLANEOUS


During a 4-yr period, 23 clinically healthy blood donors were observed to have apparently jaundiced serum and an additional nine appeared to transmit hepatitis to the recipient. These 32 patients comprised 0.04% of all blood donors and were further studied. All had raised enzyme levels indicating anicteric viral hepatitis, and mild clinical jaundice actually appeared subsequently in four subjects. Biochemical abnormalities persisted for more than 3 mo in nine subjects, and liver biopsy performed in five showed foci of necrosis in all. Australia antigen was detected in three of 12 cases.—A.A.M.


The investigations were carried out on a group of 313 subjects with a history of viral hepatitis in the last 2 yr. Australia antigen (Au) was found in the sera of nearly 4% of these subjects. More frequently it was found in the cases with a more severe course of acute disease. In patients with abnormal results of liver function tests the Au antigen was present in 14.1% of cases, while in the patients with normal results it was found in 1.4% of cases. In the group of patients treated for chronic hepatitis 2 yr after the acute episode of viral hepatitis, Au antigen was present in 25% of cases.—M.K.


The occurrence of a blood dyscrasia in association with hamartoma of the spleen has only been described in three patients. A further example occurring in a 54-yr-old woman is described. Resolution of thrombocytopenia followed splenectomy.—J.M.B.
ABSTRACTS

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